The farnesoid-X-receptor in myeloid cells controls CNS autoimmunity in an IL-10-dependent fashion.

Abstract:
Innate immune responses by myeloid cells decisively contribute to perpetuation of central nervous system (CNS) autoimmunity and their pharmacologic modulation represents a promising strategy to prevent disease progression in Multiple Sclerosis (MS). Based on our observation that peripheral immune cells from relapsing-remitting and primary progressive MS patients exhibited strongly decreased levels of the bile acid receptor FXR (farnesoid-X-receptor, NR1H4), we evaluated its potential relevance as therapeutic target for control of established CNS autoimmunity. Pharmacological FXR activation promoted generation of anti-inflammatory macrophages characterized by arginase-1, increased IL-10 production, and suppression of T cell responses. In mice, FXR activation ameliorated CNS autoimmunity in an IL-10-dependent fashion and even suppressed advanced clinical disease upon therapeutic administration. In analogy to rodents, pharmacological FXR activation in human monocytes from healthy controls and MS patients induced an anti-inflammatory phenotype with suppressive properties.
including control of effector T cell proliferation. We therefore, propose an important role of FXR in control of T cell-mediated autoimmunity by promoting anti-inflammatory macrophage responses.